REMARKS

Claims 35, 37, 43, 46, 47, 49-51, and 57 are pending.

Provisional Obviousness-Type Double Patenting

On pages 2-3 of the February 3, 2009 Final Office Action the Examiner maintained the rejection of claims 35, 37, 43, 46, 47, 49-51, and 57 under provisional non-statutory obviousness-type double patenting over claims 69, 77, 78, and 82-84 of co-pending U.S. Application No. 11/234,879. The Examiner stated that the basis for this provisional rejection is set forth at page 4 of the previous Office Action issued on May 9, 2008 and pages 6-7 of the previous Office Action of August 8, 2007. The Examiner agreed to hold the rejection in abeyance until all other issues are resolved.

Applicant acknowledges the Examiner's abeyance and maintains the position that the current rejection is provisional as the cited application is not patented or allowed. Accordingly, applicant will consider filing a terminal disclaimer, if necessary, in the current application should the claims otherwise be deemed allowable and the rejection becomes non-provisional.

Claims rejected Under 35 U.S.C. §103

Claims 35, 37, 43, 46, 49-51 and 57

The Examiner stated that claims 35, 37, 43, 46, 49-51 and 57 are rejected under 35 U.S.C. §103(a) as being unpatentable over Petersen, BE (U.S. Patent Application No. 2002/0094327; priority to November 5, 2000) in view of Hung *et al.* (U.S. Patent Application No. 2003/0171294; priority to August 13, 1999). The basis for this

rejection is set forth at pages 4-6 of the previous May 9, 2008 Office Action. The Examiner asserted that Petersen teaches administration of SDF-1 to the heart to induce migration of stem cells to that tissue and that such administration would inherently induce protection of or proliferation of cardiomyocytes. The Examiner asserted that Hung *et al.* teach administration of a growth factor (bFGF) intramyocardially or intracoronarily, and that the skilled artisan would have been motivated to combine the teachings of the cited art to localize cell migration/differentiation and tissue repair.

Applicant's Response

(1) Cited Art Does not Teach or Suggest Claimed Invention

In response, applicant respectfully traverses the Examiner's rejection. Applicant submits that the Examiner asserted on page 6 of the Final Office Action that the skilled artisan would "recognize that pluripotent stem cells that traffic to the heart tissue (due to administration of SDF-1α) will differentiate into cells, such as cardiomyocytes." However, applicant submits that the Examiner has mischaracterized the claimed invention, which recites administrating SDF-1 to induce regeneration of endogenous cardiomyocytes (i.e. by preventing apoptosis of cardiomyocytes and/or inducing proliferation of endogenous cardiomyocytes). Independent claim 35 recites administering SDF-1 in such a manner that it acts on endogenous cardiomyocytes. There is no suggestion in Petersen of this. That the SDF-1 may or may not additionally act on pluripotent stem cells, as suggested by the Examiner, is not relevant to the claimed method. Hung *et al.* in combination with Petersen does not cure this deficiency in the teachings. Moreover,

the effect on endogenous cardiomyocytes is not expected or suggested in the cited art.

Applicant also notes that at page 6 of the Final Office Action the Examiner states that "it is noted that features upon which applicant relies (i.e., administration of SDF-1 to a selected tissue in order to protect or enhance proliferation of cells endogenous to that tissue) are not recited in the rejected claim(s)." However, claim 35 clearly requires "... intramyocardially or intracoronarily administering to the subject an amount of an agent comprising a human stromal derived factor-1 effective to induce regeneration of endogenous cardiomyocytes and ...." (emphasis added). Accordingly, the invention as claimed does clearly require that SDF-1 is administered to the myocardium or the coronary circulation in an amount effective to induce regeneration of endogenous cardiomyocytes. Because the claimed method is not taught or suggested by the combined teachings of the cited art, and is not expected from it, applicant respectfully requests reconsideration and withdrawal of this rejection.

(2) Inherency

In addition, applicant submits that for inherency to be established the claimed method must be a necessary consequence of following the prior art and not just a possible or even probable outcome. In this regard, the teachings of Petersen cannot necessarily result in the claimed method because the citation does not teach intramyocardial (within the myocardium) or intracoronary (within the coronary circulation) administration of SDF-1. Accordingly, the SDF-1 could be administered to any site in the body, or even a different site in the heart, e.g., a heart chamber, the pericardium, or the

endocardium. Additionally, there is no indication that this would induce regeneration of endogenous cardiomyocytes. Accordingly, the method disclosed in Petersen does not necessarily result in the claimed method and Hung *et al.* in combination does not cure this.

Applicant further submits that inherent properties of SDF-1 cannot be used to support an argument as to why documents would be combined, because "[o]bviousness cannot be predicated on what is unknown," (See MPEP §2141.02) and also, the suggestion or motivation to combine or modify references must be present prior to an applicant's date of invention, a previously unknown inherent property cannot supply this suggestion at the required time.

Given that inherency does not apply, the Examiner must establish that the skilled person would be motivated to administer SDF-1 in the recited manner and location and, moreover, that the effect of such would be expected or predictable. However, Petersen merely suggests administering SDF-1 to a tissue (not a specific site within a tissue, let alone the myocardium or the coronary circulation) to cause non-resident stem cells to migrate to that tissue. Petersen specifically teaches that SDF-1 acts on non-resident stem cells, not on cardiomyocytes (see paragraph [0063] of Peterson). Petersen also provides no motivation or teaching to specifically administer SDF-1 to the myocardium or coronary circulation in such a manner that it induces <u>regeneration</u> of <u>endogenous</u> cardiomyocytes. Moreover, the cited combination of art does not suggest SDF-1 can cause <u>regeneration</u>.

<u>(3) Hung et al.</u>

In regard to the Examiner's citing of Hung *et al.*, the passage relied upon by the Examiner (paragraph [007]) discusses administration of an angiogenic factor to the heart such that it provides localized angiogenesis and does not induce angiogenesis in tumors. Accordingly, Hung *et al.* only teach administration of a compound that will cause blood vessels to grow towards the site of administration. Hung *et al.* fail to discuss any compound that is administered intramyocardially or intracoronarily that induces regeneration of endogenous cardiomyocytes (as opposed to blood vessels). Hung *et al.* do not even contemplate that such an effect is possible. Hung *et al.* only discuss using a growth factor to induce angiogenesis and do not contemplate SDF-1. Moreover, the Examiner does not provide any evidence that the growth factors discussed in Hung *et al.* actually have this effect. Accordingly, there is no reason to combine the teachings of Hung *et al.* to induce angiogenesis with growth factors with those of Petersen regarding attracting non-resident stem cells to a tissue.

(4) Unexpected Result

The present method provides an unexpected result when considered in view of Petersen and Hung *et al.* In particular, the application clearly exemplifies that cardiomyocytes are protected from apoptosis by SDF-1, and that SDF-1 induces endogenous cardiomyocyte proliferation/regeneration. The effect on cardiomyocyte proliferation is not contemplated by the cited combination of art and, is not expected therefrom.

Claim 47

The Examiner rejected claim 47 under 35 U.S.C. 103(a) as being unpatentable over Petersen and Hung *et al.* as applied to claims 35-37, 43, 46, 49-51, 53-57 above, and further in view of Rempel *et al.* (Clin Can Res 6: 102-111, 2000). The basis for this rejection is set forth at pages 6-7 of the previous May 9, 2008 Office Action.

The Examiner asserted that as discussed in the previous Office Action, Rempel *et al.* teaches that the SDF-1 gene encodes two isoforms, SDF-1α and SDF-1β, that arise from alternative splicing (page 102, column 2, last paragraph). Therefore, the Examiner concluded that it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of intramyocardially or intracoronarily administering SDF-1a to heart tissue as taught by Petersen and Hung *et al.* by substituting SDF-1α with SDF-1β as taught by Rempel *et al.*

Applicant's Response

In response, applicant respectfully traverses the Examiner's rejection. As discussed hereinabove Petersen and Hung *et al.* do not suggest the claimed method because the combination of these cited art does not render as obvious a method of intramyocardial (within the myocardium) or intracoronary (within the coronary circulation) administration of SDF-1 effecting endogenous cardiomyocyte regeneration. In addition, Hung *et al.* also fail to discuss any compound that is administered intramyocardially or intracoronarily that induces regeneration of endogenous cardiomyocytes (as opposed to blood vessels) and Hung *et al.* only contemplate using a growth

factor to induce angiogenesis and does not contemplate SDF-1. Therefore, it is not obvious to one skilled in the art at the time the invention was made to modify the method of intramyocardially or intracoronarily administering SDF-1α to heart tissue as allegedly taught by Petersen and Hung *et al.* by substituting SDF-1α with SDF-1β as taught by Rempel *et al.* Moreover, although it was known that SDF-1β existed at the time of Petersen (see Rempel et al., 2000, cited by the Examiner), Petersen explicitly recites SDF-1α but never recites SDF-1β. Thus, one skilled in the art seeing that Petersen only refers to SDF-1α would not immediately consider SDF-1α as replaceable with SDF-1β.

Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.